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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/904,045	07/12/2001	John W. Butcher	20709	1941

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MERCK AND CO INC
P O BOX 2000
RAHWAY, NJ 070650907

EXAMINER
CEPERLEY, MARY

ART UNIT	PAPER NUMBER
1641	5

DATE MAILED: 04/18/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/904,045	BUTCHER ET AL.	
	Examiner	Art Unit	
	Mary (Molly) E. Ceperley	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 February 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-40* is/are pending in the application.

4a) Of the above claim(s) *1-4 and 28-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *2* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

1) Applicants' election with traverse of Group IV, claims 10-27, in Paper No. 5 is acknowledged. In view of applicants' argument filed February 12, 2003, Group III, claims 5-9, drawn to a related method involving the same binding mechanism as that of the claims of Group IV, is hereby combined with Group IV for an examination on the merits. Claims 1-4 and 28-40 are withdrawn from further consideration as being drawn to non-elected inventions.

The restriction requirement is traversed on the ground(s) that the classification and fields of search are the same for the different inventions and that therefore there is no reason for restricting the claims. This is not found persuasive for the following reasons:

(1) The fields of search are not coextensive. Although certain inventions are classified in class 436, different subclasses of this class must be searched for the various inventions as indicated in the restriction requirement. Further, the searches in the technical literature are not coextensive. For example, while an examination of the method of assessing the binding of a test compound using a radioisotope involves a search for a particular radioisotopic form of a known antiarrhythmic agent, an examination of either the compound of claim 40 or the method of making the TMSO-derivative of claim 28 does not involve the search of any radioisotope.

(2) An examination of each of the groups involves different patentability considerations. For example, an examination of Group I would involve an assessment of the novelty and unobviousness of the claimed radioisotope *independent of any method of use.* An examination of Group V would involve the determination of the novelty and unobviousness of the particular combination of method steps used to prepare a TMSO-derivative and which does not involve the use of any radioisotope. An examination of Group VII would involve the determination of the novelty and unobviousness of a trimethylsilane derivative, independent of any method of use. The requirement is still deemed proper and is therefore made FINAL.

2) Although specific claims are cited in the rejections below, these rejections are also applicable to all other claims in which the noted problems/language occur.

3) The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4) Claims 5-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a) In claim 10, step 3), it is unclear what is meant by the term "known concentration of the membrane/radioligand mixture". Does the "concentration" refer to the amount of radioactivity of the "radioligand" in the "mixture"? Or does the term "concentration" imply that both the amount of "membrane" (units?) and "radioligand" (radioactivity units) are known?

b) In claim 10, step 3), it is unclear what is meant by the term "the final concentration of the membrane containing the I_{Kr} channel is predetermined". What are the units of concentration of the "membrane"? At what point in the method is the concentration considered to be "final"? It is noted that the preamble of the claim recites "the binding of a test compound to a membrane", the state of the membrane (intact {as in on the surface of a cell} or disrupted) is not specified.

c) In claim 10, steps 4) and 5), it is unclear exactly what moieties are "isolated" and "measured". Are these the same moieties described in step 7)? Steps 4) and 5) are confusing. Steps 4) and 5) read, for example, on "isolating the control vehicle" *per se* or "the compound of Formula II" in the absence of any "radioligand".

d) The term "IC_{50}" of claim 10, step 7) is undefined rendering the claim indefinite.

e) Claim 10 is incomplete in not reciting a step whereby "calculating the IC_{50}" of step 7) is correlated with "assessing the binding of a test compound" of the claim preamble. See also, claim 20.

f) Claim 5 is incomplete in not reciting a step whereby the "monitoring" is correlated to the "characterizing" of the claim preamble.

5) The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6) Claims 5-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over ***a)*** Baldwin et al (U.S. Patent No. 5,633,247) taken in combination with each of ***b)*** Chadwick et al (Circulation Research, Vol. 72, No. 3, page 707 (1993)), Fiset et al (J. Mol. Cell Cardiol., Vol. 28, page 1085 (1996)), Geonzon et al (J. Mol. Cell Cardiol., Vol. 30, page 1691 (1998), or Duff et al (Circulation Research, Vol. 77, page 718 (1995) and with ***c)*** Dean et al (Synthesis and Applications of Isotopically Labelled Compounds, Paper 140 (1994)).

Baldwin et al describe the non-radiolabeled, sulfonamide compound of formula I of instant claim 1 as being a known Class III, K^+ channel blocking antiarrythmia agent. See TABLE LVIII, Example 447 of col. 208; col. 2, lines 51-54; col. 19, lines 14-40 and 1-6.

Another Class III, K+ channel blocking antiarrythmia agent is the sulfonamide-containing drug Dofetilide (for the structure of Dofetilide, see fig. 3 of Vandenberg et al, cited by applicants on form PTO-1449). Each of references ***b)*** describes an assay which assesses the membrane K^+ channel blocking activity of radiolabeled [^{3}H] Dofetilide. See Chadwick et al: abstract, guinea pig cardiac myocytes; page 708, *[3H] Dofetilide Binding*; Fiset et al: page 1086, "[^{3}H]dofetilide equilibrium binding assay" using

myocytes, membrane homogenates, or CHO cells; Geonzon et al: Figure 1; Duff et al: page 719 "Kinetic Binding Assays". Duff et al, in the table of page 719, define I_{KR} consistent with the usage of this term in the instant specification.

Dean et al describe the use of a ^{35}S-containing sulfonamide group as being an improvement over ^{125}I and tritium labels for sulfonamide-containing ligands used in receptor binding radioassays. See the Summary, Introduction, and the last paragraph of page 800.

Given the fact that conventional radioassays which utilize the I_{Kr} channel blocking activity of Class III antiarrhythmia agents are well known (references ***b)***), it would be obvious to substitute another well known Class III antiarrhythmia agent, namely the sulfonamide compound of Baldwin et al, in the methods of references ***b)***, as claimed, with the expectation of obtaining an equivalently useful assay method. The substitution of a ^{35}S label for a ^{3}H label in the Baldwin et al compound would be an obvious improvement given the teachings of Dean et al that a ^{35}S label is preferred over a ^{3}H label in radioassays involving sulfonamide derivatives.

The additional limitations/features of the claims are either specifically described by the references (e.g. for the use of the CHO cells of claim 7, see Fiset et al; for the specific activity of claim 9, see Dean et al; for competitive binding of test compounds in a radioassay, see Fiset et al, page 1089, "Class III antiarrhythmic drugs binding to [^{3}H]dofetilide binding site") or constitute obvious variations in parameters which are routinely modified in the art (e.g. standard assay protocol of claim 10 using controls and test solutions of varying concentrations) and which have not been described as critical to the practice of the invention.

7) Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary E. (Molly) Ceperley whose telephone number is (703) 308-4239. The examiner can normally be reached from 8 a.m. to 5 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached at (703) 305-3399. The fax phone number for responses to be filed BEFORE final rejection is (703) 872-9306. The fax phone number for responses to be filed AFTER final rejection is (703) 872-9307.

Questions which are NOT RELATED TO THE EXAMINATION ON THE MERITS, should be directed to **TC 1600 CUSTOMER SERVICE at (703) 308-0198**. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

April 17, 2003

Mary E. (Molly) Ceperley
Primary Examiner
Art Unit 1641